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09/890,475	11/13/2001	Urban Johanson	MEWBURN	3312

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EXAMINER
BAUM, STUART F

ART UNIT	PAPER NUMBER
1638	10

DATE MAILED: 08/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/890,475	JOHANSON ET AL.	
	Examin r	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *11-17,19,29-34 and 37-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,18,20-28,35 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with application* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-40 are pending.

2. Applicant's election with traverse of Group I, claims 1-10, 18, 20-28, and 35-36, including the sequence from Figure 4 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that it is improper to make a lack of unity holding in a §371 application, when the international application was found to have unity. Applicants also assert that the instant invention does have a special technical feature in view of Simon et al. Applicants contend that all of the present claims are based on the use of the *Arabidopsis* "Frigida" gene, or closely related variants thereof, which are capable of conferring late flowering. Applicants state that Figure 4 shows both the genomic and cDNA sequence of presumably the *Arabidopsis* "Frigida" gene. In addition, Applicants state that the Simon et al reference describes the "Constans" gene which is capable of conferring late flowering but does not teach or suggest the "Frigida" gene which is the unifying special technical feature of the instant claims. Applicants state that claim 1 is drawn to an isolated nucleic acid obtainable from an FRI (Frigida) locus and that all of the claims explicitly require the Frigida gene (page 23, paragraphs 1-4). Finally, Applicants contend that even though nucleic acid sequences are structurally distinct, this does not preclude structurally similar nucleic acids from sharing an inventive concept. Nucleic acids which are similar, but not identical, can be drawn to the same invention.

3. This is not found persuasive because even though there was not a lack of unity for the international application, the present Examiner did follow the rules for lack of unity of invention because the originally filed claim 1 is drawn to many sequences, including variants, all from an undisclosed number of plants. Because of the multitude of sequences encompassed in claim 1,

the Simon et al reference reads on the claimed invention. In response to Applicant's argument that the reference fails to show certain features of Applicant's invention, it is noted that the features upon which Applicant relies (as stated above) are not recited in the original claim 1. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). It is noted, that according to the Figure 4 legend (page 29), Figure 4 is only a genomic sequence of the FRI gene and does not contain the cDNA sequence. In addition, Figure 4 does not contain any translation data nor any annotation data which would indicate exons, introns, start codons, or stop codons. Finally, as originally written, claim 1, reads on sequences that are not structurally similar and as such do not share an inventive concept.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 11-17, 19, 29-34, and 37-40, including SEQ ID NO:3, have been withdrawn from consideration because the claims and sequence are drawn to non-elected inventions.

5. Claims 1-10, 18, 20-28, and 35-36 are examined in the present office action.

Specification

6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See for example page 31, line 36 and page 32, line 1. See MPEP § 608.01.

7. Applicant is requested to amend the first paragraph of Example 5, page 39. It is not clear to the Examiner what is the intended meaning of the paragraph.

Claim Objections

8. Claims 4, and 9 are objected to for reading on non-elected inventions. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-10, 18, 20-28, and 35-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Rejection includes dependent claims.

In claim 1, the metes and bounds of "obtainable" have not been defined. It is unclear what DNA is not encompassed in the recitation "obtainable". All subsequent recitations of "obtainable" are also rejected.

In claim 1, the recitation "FRI locus" has not been defined. Applicants have not specifically stated what nucleic acids are encompassed in the recitation "FRI locus".

In claim 1, the metes and bounds of "capable" have not been defined. What are the limits to which something is "capable". All subsequent recitations of "capable" are also rejected.

In claim 1, the term "altering" is unclear. Applicant needs to explicitly state how flowering time has been changed. All subsequent recitations of "altering" are also rejected.

In claim 3, it is unclear whether or not the "(SEQ ID NO:1)" is intended as a claim limitation. It is suggested that the parentheses be deleted and "of SEQ ID NO:#" replace the recitation "of Fig. 6". All subsequent recitations in which a SEQ ID NO is set in parentheses are also rejected.

In claim 5, the recitation "homologous" has not been defined. The meaning of the word "homologous" includes an evolutionary component that is not defined.

In claim 8, the metes and bounds of "orthologue" have not been defined. Given the variable definitions for this term as witnessed by the Office, Applicant is requested to explicitly define the meaning of "orthologue" as it relates to Applicant's invention.

In claim 10, 2nd line, insert the word --is-- after the word "which".

In claim 23, the metes and bounds of "containing" have not been defined. It is unclear in what capacity the host cell "contains" the nucleic acid of claim 1. As an example, the host cell could "contain" the nucleic acid in a membrane bound organelle other than the nucleus or mitochondria.

In claim 24, the recitation "optionally present in a plant" is unclear. Is Applicant claiming a cell line or a transiently transformed cell of an otherwise non-transformed plant?

In claim 25, 3rd line, insert the word --and-- after the comma.

In claim 26, the phrase "which is a clone, or selfed or hybrid progeny or other descendant" is grammatically incorrect. Replacing the above phrase with "progeny thereof" will obviate the rejection.

In claim 27, the recitations "a Brassica such as" and "a culinary herb" are not plants.

In claim 27, 4th line, insert the word --and-- before the word "lettuce".

In claim 28, 1st line, insert the article --a-- before "propagule".

In claim 28, the metes and bounds of "propagule" have not been defined. It is unclear what constitutes a "propagule". How many cells constitute a propagule?

In claim 35, the metes and bounds of "influencing" and "affecting" have not been defined. Applicant needs to explicitly state how flowering time has been changed.

In claim 36, 3rd line, the second "which" should be deleted to improve the clarity of the claim.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-2, 5-10, 18, 20-28, and 35-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim an isolated nucleic acid obtainable from the FRI locus of any plant including the complement of said sequence, a variant sequence of SEQ ID NO:2 and which shares at least 60% sequence identity therewith, an allelic variant of SEQ ID NO:2, a variant VRN2 sequence from any plant other than *Arabidopsis*, or a derivative sequence of SEQ ID NO:2 wherein said sequence has additions, insertions, deletions or substitutions of any nucleotide(s). The Applicants also claim a host cell, transgenic plant and method for

influencing, affecting or altering flowering time all of which comprise transforming the host cell or plant with an above mentioned sequence.

Applicant's isolated their invention by positional cloning. The specification only discloses the nucleic acid sequence of SEQ ID NO:2 purportedly encoding SEQ ID NO:1 (page 35, Example 2, last sentence). Applicants state in the specification that SEQ ID NO:1 is a predicted amino acid sequence taken from SEQ ID NO:3, which is supposedly a cDNA sequence and the amino acid sequence is not taken from the elected sequence of SEQ ID NO:2 (page 35, Example 2). In fact, it is unclear if Applicant is in possession of any FRI encoding nucleic acid or a functional protein encoded by SEQ ID NO:2 because of Applicant's own admitted statement acknowledging the lack of exact delimitation of both the 5' and 3' untranslated regions of the coding sequence. Applicants have not provided annotation indicating the correct start, stop and splice junction codons for their predicted protein. In addition, Applicants do not disclose any specific structural, physical and/or chemical properties for the claimed sequence. Applicants do not present a description of domains that are specific to this particular protein nor domains that are important for its proper function. Applicants also do not define the nucleic acid sequence explicitly associated with the FRI locus of any plant. Given the lack of description of the before mentioned sequences, one skilled in the art would not be able to identify sequences with less than 100% sequence identity that still maintained the proper activity. The claims recite variant sequences and sequences which share at least 60% sequence identity with SEQ ID NO:1 but Applicants have not disclosed a representative number of species as encompassed by the claims. The claims encompass mutants and allelic variants and thus imply that structural variants exist in nature, yet no structural variant has been disclosed. The implication is that there is a gene and a

protein other than that disclosed which exists in nature, but the structure thereof is not known. Thus, there are insufficient relevant identifying characteristics to allow one skilled in the art to predictably determine such mutants and allelic variants from other plants and organisms, absent further guidance. Therefore, the written description requirement is not satisfied. Therefore, one skilled in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention. (See Written Description Requirement published in Federal Register/Vol.66, No. 4/ Friday, January 5, 2001/Notices; p. 1099-1111).

Enablement

11. Claims 1-10, 18, 20-28, and 35-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants claim an isolated nucleic acid obtainable from the FRI locus of any plant including the complement of said sequence, a variant sequence of SEQ ID NO:2 and which shares at least 60% sequence identity therewith, an allelic variant of SEQ ID NO:2, a variant VRN2 sequence from any plant other than *Arabidopsis*, or a derivative sequence of SEQ ID NO:2 wherein said sequence has additions, insertions, deletions or substitutions of any nucleotide(s). The Applicants also claim a host cell, transgenic plant and method for influencing, affecting or altering flowering time all of which comprise transforming the host cell or plant with an above mentioned sequence.

The claimed invention is not supported by an enabling disclosure taking into account the *In re Wands* factors (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicants have not reduced to practice their invention. Applicants have only mapped the location of the FRI locus in *Arabidopsis* and have purportedly cloned the corresponding genomic sequence as set forth in SEQ ID NO:2. Applicants have submitted a deduced amino acid sequence of SEQ ID NO:1 based on the incomplete cDNA sequence of SEQ ID NO:3 (page 35, Example 2, last sentence). Applicants have not taught how one skilled in the art can make and/or use the broadly claimed sequences to affect, influence or alter flowering time in any plant. Applicants only provide a prophetic example of using any sequence from the FRI locus of any plant, operably linked to the 35S CaMV promoter and all of which transformed into a potato plant, which supposedly delays flowering (page 40, lines 5-10).

Transforming plants with a FRI sequence or introgressing a FRI sequence into a plant, in both cases to produce a delayed flowering phenotype, produces unexpected results. Clarke et al (1994, Mol. Gen. Genet. 242 :81-89, listed in IDS) teach that different ecotypes of *Arabidopsis* possess different enhancers and suppressors that modify the late flowering phenotype produced by the FRI locus. Clarke et al states that the "Ler modifier(s) are partially dominant and that the

H51 alleles of the modifier(s) confer a degree of lateness" (page 84, left column, last sentence). Clarke et al also state that maternal or cytoplasmic factors also affect flowering time due to the FRI locus (page 88, left column, 2nd paragraph).

It cannot be predicted by one of skill in the art that nucleic acids that comprise a variant FRI sequence sequence exhibiting 60% sequence identity to SEQ ID NO:2 will encode a protein with the same activity as a protein encoded by SEQ ID NO:2. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by McConnell et al (2001, Nature 411 (6838):709-713), who teach that the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain. This change renders the protein

constitutively active and therefore creates a dominant mutation which has a drastic alteration in phenotype compared to wild-type *Arabidopsis* plants.

Applicant's claims are drawn to sequences that when transformed into a plant affect, influence or alter flowering time. Transforming plants with heterologous genes that are involved in plant development produce unpredictable results. Kano-Murakami et al (1993, FEBS 334:365-368) teach introducing the *Oryza sativa* homeobox 1 (OSH1) gene into tobacco. OSH1 is a rice homologue of the *Knotted-1* homeobox gene from maize and would be encompassed by Applicant's broad claim language. Kano-Murakami et al teach transgenic tobacco plants comprising the OSH1 gene display a "range of phenotypes which include abnormalities in leaf and petal shape as well as stem height and number" (page 365, right column, 1st paragraph).

Given the claim breadth, unpredictability and lack of guidance as stated above; given the breadth of the claims which encompass a multitude of sequences that have not been exemplified; it would require undue experimentation by one skilled in the art to identify and isolate a multitude of non-exemplified nucleic acid sequences encoding polypeptides from a multitude of non-exemplified plants, and to evaluate the ability of these sequences, variants and derivative sequences thereof having the ability to cause the claimed effects in plants transformed therewith.

2nd Enablement

12. Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claim is drawn to a method of causing or allowing recombination between a vector and host cell genome. The claim reads on inducing homologous recombination which Applicant has not reduced to practice.

Babiychuk et al (1997 Proc. Natl. Acad. Sci. 94:12722-12727) teach that homologous recombination in plants is very low (page 12722, left column) and that it is doubtful that homologous recombination will be practical in plants (page 12724, left column, 1st paragraph).

Given the unpredictability of homologous recombination in plants and the lack of guidance and examples of inducing homologous recombination, it would require undue experimentation by one skilled in the art to cause or induce homologous recombination between a vector and plant host cell.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-10, 18, 20, and 22-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Schmidt et al (1995, Science 270:480-483).

Applicants claim an isolated nucleic acid obtainable from the FRI locus of any plant, a sequence which encodes the polypeptide of SEQ ID NO:1, a variant sequence of SEQ ID NO:2 and which shares at least 60% sequence identity therewith, an allelic variant of SEQ ID NO:2 wherein the variant sequence encodes a polypeptide which is capable of specifically altering flowering time of a plant, an orthologous variant of a FRI sequence from any plant other than *Arabidopsis*, or the complement of the FRI sequence or variant sequence, a recombinant vector

comprising a FRI sequence, wherein said FRI sequence is operably linked to a promoter for transcription in a host cell, and transformed host cell.

Schmidt et al teach yeast artificial chromosome (YAC) clones comprising the DNA from chromosome 4, on which the FRI locus resides. Given that Schmidt et al had to isolate the DNA before constructing the YAC clones, and given that the FRI locus nucleic acid would be obtainable from the YAC clones and would encode the polypeptide of SEQ ID NO:1, and given that the YAC clones would comprise promoters and would be transformed into host cells, Schimdt et al anticipate the claimed invention.

14. Claims 4, 24-28, and 35-36 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated polynucleotide of SEQ ID NO:2 or a FRI nucleic acid transformed into a plant cell or any plant listed in claim 27, or method of affecting, influencing, or altering flowering time comprising transforming a plant with a FRI nucleic acid sequence.

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 703-305-6997. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 703-306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Stuart F. Baum Ph.D.

August 22, 2003

AMY J. NELSON, PH.D
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